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PULMONARY TUBERCULOSIS CHARACTERISTICS IN A PATIENT WITH TYPE 2 DIABETES MELLITUS

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Abstract

Tuberculosis (TB) and diabetes mellitus (DM) are two chronic diseases with major impact on worldwide morbidity and mortality. DM significantly increases the risk of death, therapeutic failure and relapse of TB, requiring a much more careful monitoring of these patients. In this article we present the case of a patient with type 2 DM in the stage of major chronic complications, with numerous risk factors for TB and atypical symptomatology, pulmonary X-ray showing active TB lesions. The patient did not follow the diabetologist's recommendations, discontinuing the antidiabetic treatment on his own initiative. The glycemic imbalance and chronic alcoholism caused the failure of the anti TB therapy.

key words: *pulmonary tuberculosis, diabetes mellitus, therapeutic failure*

Background

Worldwide, the prevalence of diabetes mellitus (DM) is 8.8%, with approximately 425 million people aged 20 to 79 years suffering from DM. It is estimated that by 2045 the DM prevalence will increase to 9.9%, so that the number will reach 629 million. Annually 4 million deaths are recorded as caused by DM [1]. According to the PREDATORR study (National Study on Diabetes, Prediabetes, Overweight, Obesity, Dyslipidemia, Hyperuricemia and Chronic Kidney Disease Prevalence in Romania) conducted in 2012-2014, the DM prevalence in Romania was 11.6% in persons aged 20 to 79 years [2].

On the other hand, approximately 2 billion people, which means one third of the population, are infected with Mycobacterium tuberculosis, a proportion of 5 to 15% of them developing active TB throughout their life [3,4]. In 2017, the incidence of TB was estimated at 10 million cases, and 1.3 million deaths were caused by TB. In Romania, the incidence of TB was 14,000 cases [3].

DM causes a threefold higher risk of developing active TB [5,6], with a rapidly increasing prevalence in developing countries, regions where the incidence of TB is also increased. DM-TB comorbidity is more common in men, elderly persons, married [4,7-11]. These patients are usually smokers, alcohol consumers, sedentary persons, who live in an urban

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environment, in crowded areas and in insanitary conditions [11-14]. They have a reduced level of education, a reduced economic status and no stable job [13]. They present a family history of TB, have an increased body mass index, a family history of DM and also a long duration of DM and reduced glycemic control [7,11,15]. In patients with DM, TB is usually asymptomatic, multidrug resistant and present an increased risk of therapy failure, relapse after the end of the anti TB therapy and death [16].

As a result, the association of the two diseases is a real co-epidemic, with important implications in the control of TB, requiring the implementation of effective measures for their prevention and management.

Case presentation

A 60 years old man, diagnosed with type 2 DM in 2009, was hospitalized in October 2015 in the Department of Diabetes, Nutrition and Metabolic Diseases, Emergency Clinical County Hospital Craiova for polyuria, polydipsia, paresthesias in the legs, headache, dizziness, unintentional weight loss (under 5 kg).

During the consultation, the patient related no personal history of TB, but he lived in the past in the same house with a person with active TB. He came from a rural area, was not married, he lived alone, had a reduced level of education, was unemployed and had a low income. The patient was a chronic alcohol consumer (he consumed alcohol daily) and a former smoker (he quit smoking in 2009; he smoked for 34 years approximately 40 cigarettes/day).

The personal medical history revealed type 2 DM since the age of 54, treated with oral antidiabetic drugs (Gliclazide MR 60 mg/day and Metformin 1000 mg/day), proliferative diabetic retinopathy, diabetic sensory-motor peripheral neuropathy, peripheral arterial disease, third degree arterial hypertension, angina pectoris, mixed dyslipidemia (treated with Atorvastatin 20 mg/day), obesity (with a maximum body mass index 31.63 kg/m^2) and recent second toe right foot amputation (performed three months prior to this hospitalization).

The physical examination revealed a normal body mass index (21.62 kg/m^2), stable vital signs (normal blood pressure, normal heart rate, normal temperature), no pathological changes at lungs auscultation, non-pulsatile dorsalis pedis and posterior tibial arteries and second toe right foot amputation.

The laboratory analysis yielded leukocytosis (12,200/µL), monocytosis (8.25%) and elevated erythrocyte sedimentation rate (75/105 mm), elevated hemoglobin A1c (9.6%) and high random plasma glucose level (326 mg/dL).

The chest X-ray, that showed left upper lobe infiltrative nodular opacities and cavities (Figure 1), and the positive sputum exam revealed active pulmonary TB, which imposed the patients transfer to Pneumophtisiology Clinic. It was initiated a four-drug regimen – isoniazid, rifampicin, pyrazinamide and ethambutol ($H_{300mg}R_{600mg}Z_{2000mg}E_{1600mg}$ 7/7). After 3 months, in January 2016, the anti TB therapy was reduced to rifampicin and isoniazid ($H_{200mg}R_{600mg}$ 3/7), the patients sputum exam being negative. In addition, during this period, he received regular insulin (total dose 20 units/day) in order to achieve DM control. At the moment of his discharge, the diabetologist's recommendation was long-acting basal insulin analogue (Glargine 100 U/mL – 10 units/day), Gliclazide MR 120 mg/day and Metformin 2000 mg/day.

In February 2016, the patient was readmitted in the Department of Diabetes, Nutrition and Metabolic Diseases for polyuria, polydipsia, paresthesias in the legs and bleeding left foot interdigital lesions. The antidiabetic treatment

was interrupted for 3 weeks on his own initiative. The physical examination revealed cyanotic fourth toe left foot, with sanguinolent secretions, left foot cellulitis and high local temperature. The laboratory analysis showed low red blood cells count (3,600,000/mm^3), decreased hemoglobin (11.5 g/dL), decreased hematocrit (32.6%), elevated hemoglobin A1c (10%) and high random plasma glucose level (325 mg/dL). The left foot X-ray revealed diffuse demineralization of second and third phalanges – third and fourth toe left foot. As a result, the surgeon recommended the transfer to the Surgery Clinic for wet gangrene left forefoot and the fourth toe left foot amputation was performed. The chest X-ray showed a homogeneous, triangular, diffuse contoured left upper lobe opacity (Figure 2).

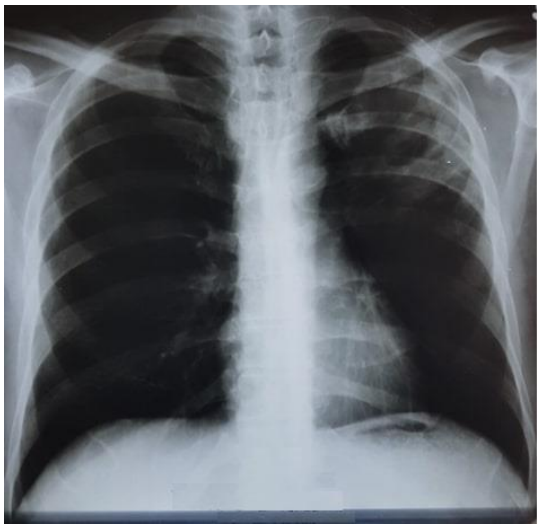

Figure 1. *Chest X-ray at TB diagnosis – left upper lobe infiltrative nodular opacities and cavities*

In April 2016, six months after the TB diagnosis, the patient was readmitted to Pneumophtisiology for cough with mucopurulent sputum, inappetence and fatigue. The laboratory analysis revealed low red blood cells count (3,340,000/mm^3), decreased hemoglobin (10.3 g/dL), decreased hematocrit (28.2%), elevated erythrocyte sedimentation rate (110/130 mm) and high random plasma glucose level (288 mg/dL). The sputum exam was positive once again and the chest X-ray showed active TB lesions (left upper lobe cavities) – therapeutic failure (Figure 3). The anti TB therapy with isoniazid, rifampicin, pyrazinamide, ethambutol and streptomycin ($H_{300mg}R_{600mg}Z_{1750mg}E_{1200mg}S_{1g}$ 7/7) was initiated.

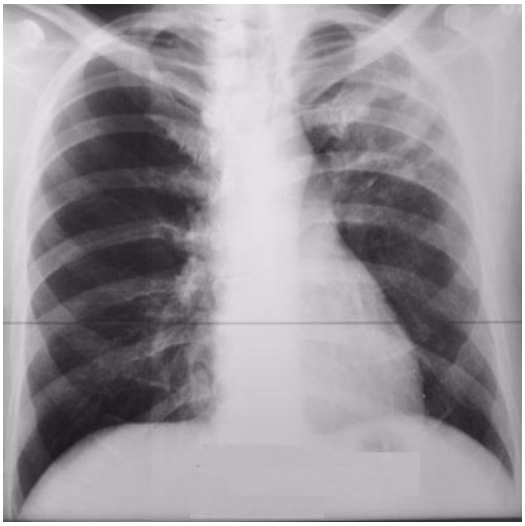

Figure 2. *Chest X-ray four months after the TB diagnosis – homogeneous, triangular, diffuse contoured left upper lobe opacity*

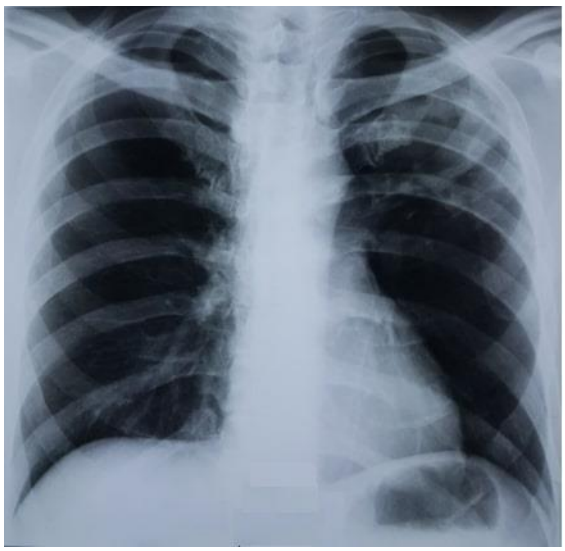

Figure 3. *Chest X-ray six months after the TB diagnosis – left upper lobe cavities (therapeutic failure)*

In June 2016, the sputum exam was negative, so the treatment with streptomycin was stopped. The patient continued the therapy with isoniazid, rifampicin, pyrazinamide and

ethambutol ($H_{300mg}R_{600mg}Z_{1750mg}E_{1200mg}$ 7/7). After one more month, in July 2016, the therapy was reduced to isoniazid, rifampicin and ethambutol ($H_{600mg}R_{600mg}E_{2000mg}$ 3/7).

In October 2016, the patient presented himself to the Outpatient Diabetes Department for the prescription. The patient was noncompliant with the recommendations, the therapy being administered inconsistently. Furthermore, he refused insulin therapy. Hemoglobin A1C was 11.4% and the treatment with Gliclazide MR 120 mg/day and Metformin 2000 mg/day has been recommended.

In December 2016, after more than a year since the initial diagnosis of TB, the patient was reevaluated. The laboratory analysis still showed a decreased hemoglobin (11.9 g/dL), a decreased hematocrit (32.3%), an elevated erythrocyte sedimentation rate (65/95 mm) and a poor glycemic control (the random plasma glucose was 276 mg/dL). The chest X-ray revealed left upper lobe fibrotic lesions and the sputum exam was negative. Thus, the patient no longer needed anti TB treatment, being considered cured.

A year and a half since the last prescription, in March 2018, the patient presented himself to the Outpatient Diabetes Department. This time, hemoglobin A1c decreased to 9.6%, but the treatment continued to be intermittently administered. The diabetologist prescribed Sitagliptin 100 mg/day in addition to Gliclazide MR 120 mg/day and Metformin 2000 mg/day and insisted on lifestyle changes and proper treatment administration.

Discussion

Patients with DM may be asymptomatic or may have atypical clinical features or radiological aspects of pulmonary TB, therefore it is necessary to consider appropriate assessment of these individuals in case of any suspicion of TB. Type 2 DM is more often associated with TB, due to its higher prevalence compared with type 1 DM.

This article presents the case of a noncompliant patient with neglected DM, disregarding the diabetologist's recommendations in terms of treatment and lifestyle, with high glycemic values, with multiple micro and macro vascular complications and multiple comorbidities. Thus, he had a significant risk of developing active pulmonary TB. Even after the TB diagnosis, the patient continued to manage his treatment intermittently, increasing the risk of therapeutic failure. Although the anti TB therapy was stopped, the patient being cured, the glycemic imbalance places the patient at increased risk of TB relapse or even death, requiring careful monitoring and compliance with the therapeutic indications.

Conclusions

The atypical characteristics of TB in this case made the patient difficult to diagnose. Also, the poor glycemic control and chronic alcoholism have negatively influenced the anti TB therapy, leading to therapeutic failure.

Thus, the DM-TB comorbidity must receive due attention, requiring bidirectional screening programs, in order to properly prevent, diagnose and treat this particular type of patients.

In addition, the presence of numerous chronic DM complications and comorbidities after such a short period of time since diagnosis implies an unfavorable prognosis, both in the long and short term.

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